II. REMARKS

Claims 1, 4, 5, 7, 8, 12, 19, 20, 22, 23 and 25-28 are pending in this application. Claims 1, 4, 5, 7, 8, 19, 20, 22, 25 and 26 are withdrawn from examination as a result of a requirement for restriction. Claims 12, 23, 27 and 28 were examined. By this Amendment, claim 28 has been amended. Support for the amendment to claim 28 is found on page 4, lines 32 to 36. Accordingly, an issue of new matter is not raised by this Amendment and entry thereof is respectfully requested.

In view of the preceding amendment and the remarks that follow, reconsideration and withdrawal of the grounds for rejection is respectfully requested.

35 U.S.C. § 102

Claims 12 and 27 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Cox et al. (1988), for the reasons of record. The Office maintained that Cox et al discloses a vaccine comprising an influenza A viral reassortant comprising nucleotides encoding the HA (wild-type), NA (wild-type), PB1 (cold-adapted), PA (cold-adapted), M (cold-adapted), and PB2 (including SEQ ID NO.: 15) polypeptides. These nucleotide sequences were linked in such a manner as to allow packaging of the reassorted polynucleotides into the virion.

In maintaining the rejection, the Office argued on page 6 of Paper No. 11 that:

> "Applicant asserts that the PB2 encoding sequence of Cox et al is not represented by sequence ID No. 15. However Figure 6 of said reference clearly indicates the nucleotides of seq ID No. 15 at positions 141 and 821, which are designated above the wild type sequence (denoted "mt"). The nucleotide at position 1933 is denoted as "x" in said mutant category, presumably indicating a sequence variation. In addition the substitution of cytosine at position 1933 changes the codon from TTG (encoding leucine) to CTG (also encoding leucine), therefore seq ID No. 15 encodes the same amino acid at this position as that in Figure 6. Accordingly Cox et al does anticipate the claimed invention." (emphasis added).

Applicants respectfully traverse. Applicants reiterate that Cox et al. fails to anticipate because it does not "contain all of the elements of the claim." See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. cir.

1986); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984); *In re Marshall*, 578 F.2d 301, 304, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978). Missing elements may not be supplied by the knowledge of one skilled in the art or the disclosure of another reference. See *Structural Rubber Prods. co. v. Park Rubber Co.*, 749 F.2d 707, 716, 223 U.S.P.Q. 1264, 1271 (Fed. Cir. 1984).

The amended claims under consideration all require the presence of mutated PB2 of the progenitor virus, the sequence of which is provided in Seq. ID No. 15. Mutated PB2 has critical differences at nucleotide positions 141, 821 and 1933 as compared to prior art sequences. In comparison to Cox et al., the base at position 1933 is thymidine while Applicants claim cytosine at position 1933 of the PB2 polynucleotide. The Office relies on an apparent printing error in the publication for maintaining the rejection stating that "[t]he nucleotide at position 1933 is denoted as "x" in said mutant category, presumably indicating a sequence variation." (emphasis added).

Applicants point out that the reference does not define this marking ("x") as a site for mutation in the cold-adapted (ca) virus. At best and without confirmation, the "x" in Figure 6 could be an asterisk, which Cox et al. describes in column 1 of page 556 (Under the RESULTS heading) to indicate that bands in two lanes of the sequencing reaction were observed at a single nucleotide position but that the darkest was read as the correct nucleotide. The legend to Figure 6 neither defines nor makes mention of it. The authors' description of the PB2 sequence makes no mention of nucleotide 1933. The authors do not list it as a mutation in Table 1 (see page 564 of Cox et al.). The authors do not identify it as a mutation that may be responsible for the cold adapted phenotype (see column 1, page 565 of Cox et al.). Additionally, an "x" would not indicate to one of skill in the art that any nucleotide may be present at that position. "X" is not a recognized abbreviation for any nucleotide ("N" is the art recognized abbreviation for any nucleotide).

Moreover, the fact that the substitution of cytosine at position 1933 changes the codon from TTG (encoding leucine) to CTG (also encoding leucine) is irrelevant in this situation. Indeed, Applicants discovered that this single change unexpectedly caused a

cascade of 163 pairing differences, from base 1888 to base 2151. Specifically, the specification notes that:

> "To assess the potential functional significance of the two nucleotide sequence differences between the *ca* and the *wt* 2(3) viruses [in the PB2 sequence], the Zuker RNA-fold algorithm and computer modeling techniques were used to predict RNA secondary structures. As shown in Figure 2, the difference at base 141 does not impinge on the predicted structure of RNA1 because it is part of an unpaired loop in both molecules; however, the change at nucleotide 1933, T in *wt* 2(3) to C in *ca* (shown by arrows in Figure 2), does affect the predicted fold of RNA1. The RNA fold of the ca virus has greater stability than the analogous fold of *wt* 2(3), as judged by its lower free energy of –736.2 compared to -733.6 for the wt 2(3) molecule. Both folds were pivoted -25° at pair 1068/1381 and 180° at pair 1675/1861 to better visualize the area of difference between the two molecules. The single base change at 1933 causes a cascade of 163 pairing differences, from based 1888 to base 2151, and thus might constitute at true cold adaptation. Similar RNA1 sequencing results were obtained for wt a/ AA/6/60 e3(4) passage virus."
>
> See page 15, line 33 to page 16 line 11 of Applicants' specification.

Accordingly, Cox et al. does not anticipate the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102.

35 U.S.C. § 103

Claims 23 and 28, stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Cox et al. (1988) in view of Maassab et al. (1982). The Office stated that Cox et al. (1988) provides methods for the production of live attenuated influenza A vaccines by genetic reassortment with a cold-adapted mutant, and that reassortant viruses containing HA and NA genes form strains H1N1 and H3N2 were disclosed. The Office opined that this teaching additionally discloses that five or six internal genes were derive from the *ca* A/Ann Arbor/6/60 parental strain.

Maassab et al. (1982) is cited by the Office for teaching that reassortants comprising six genes derived from one strain and two surface proteins derived from the wild-type parental strain were generated and that these viruses were attenuated and genetically stable (see abstract). The Office also argued that intranasal inoculation of the

A vaccine composition comprising this strain was described and that this reassortant was unable to replicate in lung tissue and grew to low titers in the nasal turbinates as compared to wild-type. The Office maintained that therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to produce a live Influenza A vaccine using cold-adapted parental strains and to incorporated these properties into a clinically relevant strain by mating and reassortant technology. The Office further maintained that one of ordinary skill in the art would have a reasonable expectation of succeeding because Cox and colleagues provide those mutations that are responsible for the cold-adapted phenotype.

Applicants respectfully traverse. The Cox et al. reference does not teach as suggested by the Office and nothing in Maassab et al. shores up the deficiencies in Cox et al. Additionally, the motivation to combine or modify the sequence of Cox et al. is missing from either Cox et al. or Maassab et al. Cox et al. clearly identified the mutations which were believed at the time the application was filed to provide the cold-adapted phenotype. Thus, a skilled artisan would not be motivated to further refine and modify the sequence.

As set forth in the response to the rejection of the claims under 35 U.S.C. § 102, the single nucleotide change at position 1933 (SEQ ID NO 15) (which does not change the coded amino acid) results in **163 pairing differences** which ultimately changes the three-dimensional structure of the virion. (See Figure 2 of the application papers). As noted in *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963):

> "From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared. But a formula is not a compound and while it may serve in a claim to identify what is being patented, as the metes and bounds of a deed identify a plot of land, the thing that is patented is not the formula but the compound identified by it. And the patentability of the thing does not depend on the similarity of its formula to that of another compound but of the similarity of the former compound to the latter. There is no basis in law for ignoring any property in making such a comparison."

Id.

For these reasons, the rejection under 35 U.S.C. § 103 is improper and therefore should be removed.

Change of Firm Name

The undersigned agent's firm name has been changed to Bingham McCutchen LLP. Applicants' agent respectfully requests the Office to change its records to reflect this change in name.

III. CONCLUSION

No fee is deemed necessary in connection with the filing of this Response. However, if the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2518**, referencing billing number **7009813001**.

However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account. Should a telephone interview advance prosecution of the subject application, the Examiner is invited to contact the undersigned at (650) 849-4950.

DATE: Sept. 12, 2003

Respectfully submitted,

By: _____
Antoinette F. Konski
Registration No.: 34,202

Bingham McCutchen LLP
Formerly McCutchen, Doyle, Brown & Enersen, LLP
Three Embarcadero Center, Suite 1800
San Francisco, California 94111
Telephone: (650) 849-4950
Telefax: (650) 849-4800

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Herlocher, M L
Maassab, H F
Webster, R G

(B) TITLE: Molecular and biological changes in the cold adapted master strain A/AA/6/60 (H2N2) influenza virus

(C) JOURNAL: Proceedings of the National Academy of Sciences of the USA

(G) DATE: 1993

(K) RELEVANT RESIDUES IN SEQ ID NO:15: FROM 1 TO 2341

(x) PUBLICATION INFORMATION:

(A) AUTHORS: Cox, N J
Kitame, F
Kendal, A P
Maassab, H F
Naeve, C

(B) TITLE: Identification of sequence changes in the cold-adapted live attenuated influenza vaccine strain, A/Ann Arbor/6/60(H2N2)

(C) JOURNAL: Virology

(D) VOLUME: 167

(F) PAGES: 554-567

(G) DATE: 1988

(K) RELEVANT RESIDUES IN SEQ ID NO:15: FROM 1 TO 2341

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

```
AGCGAAAGCA GGUCAAUUAU AUUCAAU AUG GAA AGA AUA AAA GAA CUA CGG          51
                               Met Glu Arg Ile Lys Glu Leu Arg
                                 1               5

AAU CUG AUG UCG CAG UCU CGC ACU CGC GAG AUA CUA ACA AAA ACC ACA          99
Asn Leu Met Ser Gln Ser Arg Thr Arg Glu Ile Leu Thr Lys Thr Thr
     10                  15                  20

GUG GAC CAU AUG GCC AUA AUU AAG AAG UAC ACA UCA GGG AGG CAG GAA         147
Val Asp His Met Ala Ile Ile Lys Lys Tyr Thr Ser Gly Arg Gln Glu
 25                  30                  35                  40
```

```
AAG AAC CCG UCA CUU AGG AUG AAA UGG AUG AUG GCA AUG AAA UAU CCG          195
Lys Asn Pro Ser Leu Arg Met Lys Trp Met Met Ala Met Lys Tyr Pro
                    45                  50                  55

AUU ACA GCC GAC AAG AGG AUA ACA GAA AUG AUU CCU GAG AGA AAU GAG          243
Ile Thr Ala Asp Lys Arg Ile Thr Glu Met Ile Pro Glu Arg Asn Glu
                60                  65                  70

CAA GGG CAA ACU CUA UGG AGU AAA AUG AGU GAU GCC GGA UCG GAU CGU          291
Gln Gly Gln Thr Leu Trp Ser Lys Met Ser Asp Ala Gly Ser Asp Arg
            75                  80                  85

GUG AUG GUA UCA CCU CUG GCU GUG ACA UGG UGG AAU AGA AAU GGA CCA          339
Val Met Val Ser Pro Leu Ala Val Thr Trp Trp Asn Arg Asn Gly Pro
        90                  95                  100

AUG ACA AGU ACG GUU CAU UAU CCA AAA AUC UAC AAA ACU UAU UUU GAG          387
Met Thr Ser Thr Val His Tyr Pro Lys Ile Tyr Lys Thr Tyr Phe Glu
105                 110                 115                 120

AAA GUC GAA AGG UUA AAA CAU GGA ACC UUU GGC CCU GUC CAU UUU AGA          435
Lys Val Glu Arg Leu Lys His Gly Thr Phe Gly Pro Val His Phe Arg
                125                 130                 135

AAC CAA GUC AAA AUA CGC CGA AGA GUU GAC AUA AAU CCU GGU CAU GCA          483
Asn Gln Val Lys Ile Arg Arg Arg Val Asp Ile Asn Pro Gly His Ala
            140                 145                 150

GAC CUC AGU GCC AAG GAG GCA CAG GAU GUA AUC AUG GAA GUU GUU UUC          531
Asp Leu Ser Ala Lys Glu Ala Gln Asp Val Ile Met Glu Val Val Phe
        155                 160                 165

CCU AAC GAA GUG GGG GCC AGG AUA CUA ACG UCG GAA UCG CAA UUA ACA          579
Pro Asn Glu Val Gly Ala Arg Ile Leu Thr Ser Glu Ser Gln Leu Thr
    170                 175                 180

AUA ACC AAA GAG AAA AAA GAA GAA CUC CAG GAU UGC AAA AUU UCA CCU          627
Ile Thr Lys Glu Lys Lys Glu Glu Leu Gln Asp Cys Lys Ile Ser Pro
185                 190                 195                 200

UUG AUG GUU GCG UAC AUG UUA GAG AGA GAA CUU GUC CGA AAA ACG AGA          675
Leu Met Val Ala Tyr Met Leu Glu Arg Glu Leu Val Arg Lys Thr Arg
                205                 210                 215

UUU CUC CCA GUU GCU GGU GGA ACA AGC AGU GUG UAC AUU GAA GUG UUG          723
Phe Leu Pro Val Ala Gly Gly Thr Ser Ser Val Tyr Ile Glu Val Leu
            220                 225                 230

CAC UUG ACU CAA GGA ACA UGC UGG GAA CAG AUG UAC ACU CCA GGU GGA          771
His Leu Thr Gln Gly Thr Cys Trp Glu Gln Met Tyr Thr Pro Gly Gly
        235                 240                 245

GAA GUG AGG AAU GAU GAU GUU GAU CAA AGU CUA AUU AUU GCA GCC AGG          819
Glu Val Arg Asn Asp Asp Val Asp Gln Ser Leu Ile Ile Ala Ala Arg
    250                 255                 260
```

```
AGC AUA GUG AGA AGA GCA GCA GUA UCA GCA GAU CCA CUA GCA UCU UUA          867
Ser Ile Val Arg Arg Ala Ala Val Ser Ala Asp Pro Leu Ala Ser Leu
265                 270                 275                 280

UUG GAG AUG UGC CAC AGC ACA CAG AUU GGC GGG ACA AGG AUG GUG GAC          915
Leu Glu Met Cys His Ser Thr Gln Ile Gly Gly Thr Arg Met Val Asp
                285                 290                 295

AUU CUU AGG CAG AAC CCA ACA GAA GAG CAA GCU GUG GAA AUA UGC AAG          963
Ile Leu Arg Gln Asn Pro Thr Glu Glu Gln Ala Val Glu Ile Cys Lys
            300                 305                 310

GCU GCA AUG GGA CUG AGG AUC AGC UCA UCC UUC AGU UUU GGC GGG UUC         1011
Ala Ala Met Gly Leu Arg Ile Ser Ser Ser Phe Ser Phe Gly Gly Phe
        315                 320                 325

ACA UUU AAG AGA ACA AGC GGA UCA UCA GUC AAG AGA GAG GAA GAA GUG         1059
Thr Phe Lys Arg Thr Ser Gly Ser Ser Val Lys Arg Glu Glu Glu Val
    330                 335                 340

CUU ACG GGC AAU CUU CAA ACA UUG AAA AUA AGG GUG CAU GAG GGA UAC         1107
Leu Thr Gly Asn Leu Gln Thr Leu Lys Ile Arg Val His Glu Gly Tyr
345                 350                 355                 360

GAG GAG UUC ACA AUG GUU GGG AAA AGG GCA ACA GCU AUA CUC AGA AAA         1155
Glu Glu Phe Thr Met Val Gly Lys Arg Ala Thr Ala Ile Leu Arg Lys
                365                 370                 375

GCA ACC AGG AGA UUG AUU CAG CUG AUU GUG AGU GGA AGA GAC GAA CAG         1203
Ala Thr Arg Arg Leu Ile Gln Leu Ile Val Ser Gly Arg Asp Glu Gln
            380                 385                 390

UCG AUA GCU GAA GCA AUA AUU GUG GCC AUG GUA UUU UCA CAA GAA GAU         1251
Ser Ile Ala Glu Ala Ile Ile Val Ala Met Val Phe Ser Gln Glu Asp
        395                 400                 405

UGU AUG AUA AAA GCA GUU AGA GGU GAU CUG AAU UUC GUU AAU AGG GCA         1299
Cys Met Ile Lys Ala Val Arg Gly Asp Leu Asn Phe Val Asn Arg Ala
    410                 415                 420

AAU CAG CGA UUG AAU CCC AUG CAU CAA CUU UUA AGA CAU UUU CAG AAG         1347
Asn Gln Arg Leu Asn Pro Met His Gln Leu Leu Arg His Phe Gln Lys
425                 430                 435                 440

GAU GCG AAA GUG CUU UUU CAA AAU UGG GGA AUU GAA CAU AUC GAC AAU         1395
Asp Ala Lys Val Leu Phe Gln Asn Trp Gly Ile Glu His Ile Asp Asn
                445                 450                 455

GUG AUG GGA AUG AUU GGG GUA UUA CCA GAC AUG ACU CCA AGC ACA GAG         1443
Val Met Gly Met Ile Gly Val Leu Pro Asp Met Thr Pro Ser Thr Glu
            460                 465                 470

AUG UCA AUG AGA GGG GUA AGA GUC AGC AAA AUG GGC GUA GAU GAA UAC         1491
Met Ser Met Arg Gly Val Arg Val Ser Lys Met Gly Val Asp Glu Tyr
        475                 480                 485
```

```
UCC AGC GCG GAG AGA GUA GUG GUG AGC AUU GAC CGG UUU UUG AGA GUU                1539
Ser Ser Ala Glu Arg Val Val Val Ser Ile Asp Arg Phe Leu Arg Val
    490                 495                 500

CGA GAC CAA CGA GGA AAU GUA CUA CUA UCU CCU GAG GAG GUC AGU GAA                1587
Arg Asp Gln Arg Gly Asn Val Leu Leu Ser Pro Glu Glu Val Ser Glu
505                 510                 515                 520

ACA CAG GGA ACA GAG AAA CUG ACA AUA ACU UAC UCA UCG UCA AUG AUG                1635
Thr Gln Gly Thr Glu Lys Leu Thr Ile Thr Tyr Ser Ser Ser Met Met
                525                 530                 535

UGG GAG AUU AAU GGC CCU GAG UCA GUG UUG GUC AAU ACC UAU CAG UGG                1683
Trp Glu Ile Asn Gly Pro Glu Ser Val Leu Val Asn Thr Tyr Gln Trp
            540                 545                 550

AUC AUC AGA AAC UGG GAA ACU GUU AAA AUU CAG UGG UCU CAG AAU CCU                1731
Ile Ile Arg Asn Trp Glu Thr Val Lys Ile Gln Trp Ser Gln Asn Pro
        555                 560                 565

ACA AUG CUA UAC AAU AAA AUG GAA UUU GAG CCA UUU CAG UCU UUA GUU                1779
Thr Met Leu Tyr Asn Lys Met Glu Phe Glu Pro Phe Gln Ser Leu Val
    570                 575                 580

CCU AAG GCC AUU AGA GGC CAA UAC AGU GGG UUU GUU AGG ACU CUA UUC                1827
Pro Lys Ala Ile Arg Gly Gln Tyr Ser Gly Phe Val Arg Thr Leu Phe
585                 590                 595                 600

CAA CAA AUG AGG GAU GUA CUU GGG ACA UUU GAU ACC ACC CAG AUA AUA                1875
Gln Gln Met Arg Asp Val Leu Gly Thr Phe Asp Thr Thr Gln Ile Ile
                605                 610                 615

AAA CUU CUU CCC UUU GCA GCC GCC CCA CCA AAG CAA AGU AGA AUG CAG                1923
Lys Leu Leu Pro Phe Ala Ala Ala Pro Pro Lys Gln Ser Arg Met Gln
            620                 625                 630

UUC UCU UCA CUG ACU GUG AAU GUG AGG GGA UCA GGA AUG AGA AUA CUU                1971
Phe Ser Ser Leu Thr Val Asn Val Arg Gly Ser Gly Met Arg Ile Leu
        635                 640                 645

GUA AGG GGC AAU UCU CCU AUA UUC AAC UAC AAC AAG ACC ACU AAG AGA                2019
Val Arg Gly Asn Ser Pro Ile Phe Asn Tyr Asn Lys Thr Thr Lys Arg
    650                 655                 660

CUA ACA AUU CUC GGA AAG GAU GCU GGC ACU UUA ACU GAA GAC CCA GAU                2067
Leu Thr Ile Leu Gly Lys Asp Ala Gly Thr Leu Thr Glu Asp Pro Asp
665                 670                 675                 680

GAA GGC ACA UCU GGA GUG GAG UCC GCU GUU CUG AGA GGA UUC CUC AUU                2115
Glu Gly Thr Ser Gly Val Glu Ser Ala Val Leu Arg Gly Phe Leu Ile
                685                 690                 695

CUG GGC AAA GAA GAU AGG AGA UAU GGA CCA GCA UUA AGC AUC AAU GAA                2163
Leu Gly Lys Glu Asp Arg Arg Tyr Gly Pro Ala Leu Ser Ile Asn Glu
            700                 705                 710
```

```
CUG AGU AAC CUU GCG AAA GGA GAA AAG GCU AAU GUA CUA AUU GGG CAA        2211
Leu Ser Asn Leu Ala Lys Gly Glu Lys Ala Asn Val Leu Ile Gly Gln
        715                 720                 725

GGA GAC GUG GUG UUG GUA AUG AAA CGA AAA CGG AAC UCU AGC AUA CUU        2259
Gly Asp Val Val Leu Val Met Lys Arg Lys Arg Asn Ser Ser Ile Leu
    730                 735                 740

ACU GAC AGC CAG ACA GCG ACC AAA AGG AUU CGG AUG GCC AUC AAU             2304
Thr Asp Ser Gln Thr Ala Thr Lys Arg Ile Arg Met Ala Ile Asn
745                 750                 755

UAAUGUUGAA UAGUUUAAAA ACGACCUUGU UUCUACU                               2341
```

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 759 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

```
Met Glu Arg Ile Lys Glu Leu Arg Asn Leu Met Ser Gln Ser Arg Thr
 1               5                  10                  15

Arg Glu Ile Leu Thr Lys Thr Thr Val Asp His Met Ala Ile Ile Lys
            20                  25                  30

Lys Tyr Thr Ser Gly Arg Gln Glu Lys Asn Pro Ser Leu Arg Met Lys
        35                  40                  45

Trp Met Met Ala Met Lys Tyr Pro Ile Thr Ala Asp Lys Arg Ile Thr
    50                  55                  60

Glu Met Ile Pro Glu Arg Asn Glu Gln Gly Gln Thr Leu Trp Ser Lys
65                  70                  75                  80

Met Ser Asp Ala Gly Ser Asp Arg Val Met Val Ser Pro Leu Ala Val
                85                  90                  95

Thr Trp Trp Asn Arg Asn Gly Pro Met Thr Ser Thr Val His Tyr Pro
            100                 105                 110

Lys Ile Tyr Lys Thr Tyr Phe Glu Lys Val Glu Arg Leu Lys His Gly
        115                 120                 125
```